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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,748	03/30/2005	Berislav V Zlokovic	GRT/4061-32	1588

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EXAMINER	
KOLKER, DANIEL E	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
12/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,748	ZLOKOVIC ET AL.	
	Examiner	Art Unit	
	DANIEL KOLKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,13,16-18,25,29,30 and 34-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,13,16-18,25,29,30 and 34-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/16/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 11 September 2009 have been entered. Claims 6, 13, 16-18, 25, 29-30, and 34-38 are pending and under examination.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11 September 2009 has been entered.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6, 13, 16-18, 25, 29-30, and 34-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bertilsson (U.S. Patent Application Publication 2003/0165485) in view of Hung (U.S. Patent Application Publication 2003/0060415).

This rejection stands for the reasons previously made of record and explained in further detail below. The claims are drawn to methods comprising administering human protein S (each of independent claims 6, 25, and 30) to human patients who have suffered a stroke (claims 6 and 30, note cerebral ischemia recited in claim 6 is a form of stroke) or neurotrauma

(claim 25, which is broad but clearly includes stroke, as stroke leads to trauma for neurons). The preambles of the independent claims are drawn to “protecting one or more cell types” (claim 6) or to "treating" neurotrauma or stroke (claims 25 and 30 respectively). However the preamble need not necessarily be given patentable weight, especially in those circumstances where it recites an intended use or effect of the claimed invention and the body of the claim fully defines the invention; see for example MPEP § 2111.02, particularly subsection (II). Thus the claims are construed as requiring a single starting material (human protein S) and a single step (administering this protein to the relevant patient population).

Bertilsson teaches treating stroke in human patients by administering protein S; see for example paragraph [0016] for teaching that protein S is to be used for treating “a disease or disorder of the central nervous system in a mammal in need of such treatment". CNS diseases to be treated include ischemic disorders such as stroke, as well as trauma (see paragraph [0139], in particular the sentence bridging pp. 14-15. While mammals in general are to be treated, humans in particular are taught by Bertilsson as appropriate subjects; see paragraph [0140]. Bertilsson does not teach administration of protein C or activated protein C, and does not suggest such administration. In fact, the examiner is unable to find mention of “protein C” or “APC” even once within this reference. The only difference between independent claims 6, 25, and 30 is that Bertilsson does not explicitly require administration of human protein S, rather the document is generic and implies that any form of “protein S” can be used.

As set forth previously, Hung teaches administration of human protein S is therapeutic for human patients; see for example paragraph[0041] and claims 1 and 48 for teaching that protein S should be administered for treating certain medical conditions, as well as paragraph [0085] for teaching that human forms of the protein are preferred. However while Hung teaches treatment of ischemia of the heart (paragraphs [0011], [0019], [0023], and [0025] for example) the reference does not teach treatment of stroke or cerebral ischemia or neurotrauma as required by the independent claims.

Nevertheless, it would have been obvious to one of ordinary skill in the art to modify the teachings of Bertilsson by selecting human protein S taught by Hung, thereby arriving at the invention of claims 6, 25, and 30. Choosing the human form of protein S would have been obvious, as it would reduce the likelihood of immune rejection of a foreign protein.

Applicant argued that the invention as claimed would not have been obvious. Specifically, in the remarks filed 11 September 2009, applicant made the following points:

1) one of ordinary skill in the art would not have found Bertilsson's statements that protein S could be used to be persuasive, as Gas6 and protein S would not be expected to have the same activity, so substituting one for the other would not have been obvious.

2) nothing in Bertilsson teaches or suggests neuroprotection, which is required for the claimed invention, and neuroprotection and neurogenesis are different mechanisms.

3) nothing in Hung suggests treating neurological conditions, and the reference in fact teaches away from such by requiring administration to the pericardial space.

With respect to 1), applicant appears to be arguing that although Bertilsson shows effective use of Gas6, since the methods of using protein S were not reduced to practice and because the art suggests that Gas6 is a ligand for the receptor Sky but protein S is not, one of skill in the art would not have had a reasonable expectation of success in using protein S. The examiner disagrees with this reasoning. First, nowhere in Bertilsson is there any suggestion that protein S will not work. Although the working examples provided in the publication (pp. 19-28) deal with Gas6 rather than protein S, Bertilsson states that the thing that is common to all reagents to be used in his methods is that they all regulate the phosphorylation of Dab1 (paragraph [0016] for example). Applicant suggests that protein S and Gas6 act through different receptors, so they would not be expected to have the same effect, namely regulating Dab1 phosphorylation. According to applicant, Nagano et al. 1996 (cited in IDS filed 16 September 2009) teach that protein S does not activate Sky.

The examiner acknowledges that there had been some controversy in the mid-1990s as to whether or not protein S activates Sky. Sky is a synonym for Tyro3 (see Lan et al. 2000 Blood 95:633-638, p. 633 second paragraph and Bertilsson paragraph [0060]). Bertilsson teaches that protein S activates Tyro3 and this has been confirmed by Lan; see for example Figure 7. By 2000, it was recognized that protein S activates Tyro3 (Sky). Thus one of skill in the art would have expected that since both Gas6 and protein S activate Sky/Tyro3, they would both work in the method of Bertilsson, even though the reference only provides data about Gas6.

With respect to 2) the only recitation of neuroprotection is in the preamble of claim 6. Although Bertilsson did not measure neuroprotection, since the reference teaches administering almost exactly the same product as claimed (recall Bertilsson differs from claim 6 only in that it doesn't explicitly teach human protein S) to the same patient population (including patients with cerebral ischemia and stroke), the recited effects such as neuroprotection will necessarily occur.

If applicant truly believes that the data set forth in Bertilsson are incompatible with neuroprotection, then applicant may want to amend the claims to recite certain features of the method which are non-obvious over Bertilsson. These might include, for example, administration of protein S for a duration or at a dose that is well beyond the ranges that Bertilsson teaches are effective. However in making such an amendment, applicant should be sure that the claims are supported by the originally-filed disclosure.

With respect to 3) above, the examiner acknowledges that Hung does not teach treating the conditions recited in the claims. In fact, if the reference did teach treatment of stroke, this may be sufficient for a rejection under 35 USC 102 rather than 35 USC 103. However, the reference provides evidence that human protein S was known at the time the invention was made, and furthermore provides a reasonable expectation of success, since it shows that protein S can be used to treat other types of ischemia and reperfusion injuries, as recited in claim 6. With respect to the point that Hung teaches away from the claimed invention, this is not persuasive. Hung does in fact teach administration to the pericardium. But that is not a teaching away from the present methods, which are drawn to administration to a human. Rather the teaching to administer protein S to the pericardium is merely a specific embodiment falling within the scope of the present claims which are generic as to where the protein should be administered.

For at least the reasons above, the rejection over independent claims 6, 25, and 30 is maintained. Applicant did not traverse the examiner's determination that the dependent claims are also rendered obvious. Note claims 13 , 29, and 34 all are drawn to patients without protein S deficiency; no such deficiency is mentioned in either reference (Bertilsson or Hung). Claim 16 only requires that the protein S be administered after diagnosis of disease, such as after the patient has been identified as having had a stroke. Claims 17-18 and new claims 35-38 recite effects which will necessarily occur upon administration of the protein.

Conclusion

4. No claim is allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL KOLKER whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel E. Kolker/
Primary Examiner, Art Unit 1649
December 28, 2009